

| | |
|---|-----|
| GGAATTCCGT AGTGGGAGGC CGGGCACAGC CTTCCTGTGT GGTTTTACCG CCCAGAGAGC | 60 |
| * ** | |
| GTC ATG GAC CTG GGG AAA CCA ATG AAA AGC GTG CTG GTG GTG GCT CTC | 108 |
| Met Asp Leu Gly Lys Pro Met Lys Ser Val Leu Val Val Ala Leu | |
| 1 5 10 15 | |
| CTT GTC ATT TTC CAG GTA TGC CTG TGT CAA GAT GAG GTC ACG GAC GAT | 156 |
| Leu Val Ile Phe Gln Val Cys Leu Cys Gln Asp Glu Val Thr Asp Asp | |
| 20 25 30 | |
| TAC ATC GGA GAC AAC ACC ACA GTG GAC TAC ACT TTG TTC GAG TCT TTG | 204 |
| Tyr Ile Gly Asp Asn Thr Thr Val Asp Tyr Thr Leu Phe Glu Ser Leu | |
| 35 CHO ### ### 40 45 | |
| TGC TCC AAG AAG GAC GTG CGG AAC TTT AAA GCC TGG TTC CTC CCT ATC | 252 |
| Cys Ser Lys Lys Asp Val Arg Asn Phe Lys Ala Trp Phe Leu Pro Ile | |
| 50 55 60 | |
| ATG TAC TCC ATC ATT TGT TTC GTG GGC CTA CTG GGC AAT GGG CTG GTC | 300 |
| Met Tyr Ser Ile Ile Cys Phe Val Gly Leu Leu Gly Asn Gly Leu Val | |
| 65 70 75 | |
| GTG TTG ACC TAT ATC TAT TTC AAG AGG CTC AAG ACC ATG ACC GAT ACC | 348 |
| Val Leu Thr Tyr Ile Tyr Phe Lys Arg Leu Lys Thr Met Thr Asp Thr | |
| 80 85 90 95 | |
| TAC CTG CTC AAC CTG GCG GTG GCA GAC ATC CTC TTC CTC CTG ACC CTT | 396 |
| Tyr Leu Leu Asn Leu Ala Val Ala Asp Ile Leu Phe Leu Leu Thr Leu | |
| 100 105 110 | |
| CCC TTC TGG GCC TAC AGC GCG GCC AAG TCC TGG GTC TTC GGT GTC CAC | 444 |
| Pro Phe Trp Ala Tyr Ser Ala Ala Lys Ser Trp Val Phe Gly Val His | |
| 115 120 125 | |
| TTT TGC AAG CTC ATC TTT GCC ATC TAC AAG ATG AGC TTC TTC AGT GGC | 492 |
| Phe Cys Lys Leu Ile Phe Ala Ile Tyr Lys Met Ser Phe Phe Ser Gly | |
| 130 135 140 | |
| ATG CTC CTA CTT CTT TGC ATC AGC ATT GAC CGC TAC GTG GCC ATC GTC | 540 |
| Met Leu Leu Leu Leu Cys Ile Ser Ile Asp Arg Tyr Val Ala Ile Val | |
| 145 150 155 | |

FIG.1A-1

| | |
|---|------|
| CAG GCT GTC TCA GCT CAC CGC CAC CGT GCC CGC GTC CTT CTC ATC AGC Gln Ala Val Ser Ala His Arg His Arg Ala Arg Val Leu Leu Ile Ser 160 165 170 175 | 588 |
| AAG CTG TCC TGT GTG GGC AGC GCC ATA CTA GCC ACA GTG CTC TCC ATC Lys Leu Ser Cys Val Gly Ser Ala Ile Leu Ala Thr Val Leu Ser Ile 180 185 190 | 636 |
| CCA GAG CTC CTG TAC AGT GAC CTC CAG AGG AGC AGC AGT GAG CAA GCG Pro Glu Leu Leu Tyr Ser Asp Leu Gln Arg Ser Ser Ser Glu Gln Ala 195 200 205 | 684 |
| ATG CGA TGC TCT CTC ATC ACA GAG CAT GTG GAG GCC TTT ATC ACC ATC Met Arg Cys Ser Leu Ile Thr Glu His Val Glu Ala Phe Ile Thr Ile 210 215 220 | 732 |
| CAG GTG GCC CAG ATG GTG ATC GGC TTT CTG GTC CCC CTG CTG GCC ATG Gln Val Ala Gln Met Val Ile Gly Phe Leu Val Pro Leu Leu Ala Met 225 230 235 | 780 |
| AGC TTC TGT TAC CTT GTC ATC ATC CGC ACC CTG CTC CAG GCA CGC AAC Ser Phe Cys Tyr Leu Val Ile Ile Arg Thr Leu Leu Gln Ala Arg Asn 240 245 250 255 | 828 |
| TTT GAG CGC AAC AAG GCC ATC AAG GTG ATC ATC GCT GTG GTC GTG GTC Phe Glu Arg Asn Lys Ala Ile Lys Val Ile Ile Ala Val Val Val Val 260 265 270 | 876 |
| TTC ATA GTC TTC CAG CTG CCC TAC AAT GGG GTG GTC CTG GCC CAG ACG Phe Ile Val Phe Gln Leu Pro Tyr Asn Gly Val Val Leu Ala Gln Thr 275 280 285 | 924 |
| GTG GCC AAC TTC AAC ATC ACC AGT AGC ACC TGT GAG CTC AGT AAG CAA Val Ala Asn Phe Asn Ile Thr Ser Ser Thr Cys Glu Leu Ser Lys Gln 290 CHO ### ### 295 300 | 972 |
| CTC AAC ATC GCC TAC GAC GTC ACC TAC AGC CTG GCC TGC GTC CGC TGC Leu Asn Ile Ala Tyr Asp Val Thr Tyr Ser Leu Ala Cys Val Arg Cys 305 310 315 | 1020 |

FIG.1A-2

| | |
|---|------|
| TGC GTC AAC CCT TTC TTG TAC GCC TTC ATC GGC GTC AAG TTC CGC AAC | 1068 |
| Cys Val Asn Pro Phe Leu Tyr Ala Phe Ile Gly Val Lys Phe Arg Asn | |
| 320 325 330 335 | |
| GAT ATC TTC AAG CTC TTC AAG GAC CTG GGC TGC CTC AGC CAG GAG CAG | 1116 |
| Asp Ile Phe Lys Leu Phe Lys Asp Leu Gly Cys Leu Ser Gln Glu Gln | |
| 340 345 350 | |
| CTC CGG CAG TGG TCT TCC TGT CGG CAC ATC CGG CGC TCC TCC ATG AGT | 1164 |
| Leu Arg Gln Trp Ser Ser Cys Arg His Ile Arg Arg Ser Ser Met Ser | |
| 355 360 365 | |
| GTG GAG GCC GAG ACC ACC ACC ACC TTC TCC CCA TAGGCGACTC TTCTGCCTGG | 1217 |
| Val Glu Ala Glu Thr Thr Thr Thr Phe Ser Pro *** | |
| 370 375 | |
| ACTAGAGGGA CCTCTCCCAG GGTCCCTGGG GTGGGGATAG GGAGCAGATG CAATGACTCA | 1277 |
| GGACATCCCC CCGCCAAAAG CTGCTCAGGG GAAAAAGCAG CTCTCCCCTC AGAGTGCAAG | 1337 |
| CCCCTGCTCC AGAAGATAGC TTCACCCCAA TCCCAGCTAC CTCAACCAAT GCCAAAAAAA | 1397 |
| GACAGGGCTG ATAAGCTAAC ACCAGACAGA CAACACTGGG AAACAGAGGC TATTGTCCCC | 1457 |
| TAAACCAAAA ACTGAAAGTG AAAGTCCAGA AACTGTTCCT ACCTGCTGGA GTGAAGGGGC | 1517 |
| CAAGCAGGGT GAGTGCAAGG GCGGTGGGAG TGGCCTGAAG AGTCCTCTGA ATGAACCTTC | 1577 |
| TGGCCTCCCA CAGACTCAAA TGCTCAGACC AGCTCTTCCG AAAACCAGGC CTTATCTCCA | 1637 |
| AGACCAGAGA TAGTGGGGAG ACTTCTTGGC TTGGTGAGGA AAAGCGGACA TCAGCTGGTC | 1697 |
| AAACAAACTC TCTGAACCCC TCCCTCCATC GTTTTCTTCA CTGTCTCCA AGCCAGCGGG | 1757 |
| AATGGCAGCT GCCACGCCGC CCTAAAAGCA CACTCATCCC CTCATTGCC GCGTCGCCCT | 1817 |
| CCCAGGCTCT CAACAGGGGA GAGTGTGGTG TTTCTGCAG GCCAGGCCAG CTGCCTCCGC | 1877 |
| GTGATCAAAG CCACACTCTG GGCTCCAGAG TGGGGATGAC ATGCACTCAG CTCTTGGCTC | 1937 |

FIG.1A-3

| | |
|---|------|
| CACTGGGATG GGAGGAGAGG ACAAGGGAAA TGTCAGGGGC GGGGAGGGTG ACAGTGGCCG | 1997 |
| CCCAAGGCCA CGAGCTTGTT CTTTGTTCIT TGTCACAGGG ACTGAAAACC TCTCCTCATG | 2057 |
| TTCTGCTTTC GATTCGTAA GAGAGCAACA TTTTACCCAC ACACAGATAA AGTTTTCCCT | 2117 |
| TGAGGAAACA ACAGCTTTAA AAAAAAAAAA GGAATTC | 2154 |

FIG.1A-4

GGAATTCCT GATATACACC TGGACCACCA CCA ATG GAT ATA CAA ATG GCA AAC 54

* **

Met Asp Ile Gln Met Ala Asn

1

5

AAT TTT ACT CCG CCC TCT GCA ACT CCT CAG GGA AAT GAC TGT GAC CTC 102

Asn Phe Thr Pro Pro Ser Ala Thr Pro Gln Gly Asn Asp Cys Asp Leu

CHO ### ###

10

15

20

TAT GCA CAT CAC AGC AGC GCC AGG ATA GTA ATG CCT CTG CAT TAC AGC 150

Tyr Ala His His Ser Thr Ala Arg Ile Val Met Pro Leu His Tyr Ser

25

30

35

CTC GTC TTC ATC ATT GGG CTC GTG GGA AAC TTA CTA GCC TTG GTC GTC 198

Leu Val Phe Ile Ile Gly Leu Val Gly Asn Leu Leu Ala Leu Val Val

40

45

50

55

ATT GTT CAA AAC AGG AAA AAA ATC AAC TCT ACC ACC CTC TAT TCA ACA 246

Ile Val Gln Asn Arg Lys Lys Ile Asn Ser Thr Thr Leu Tyr Ser Thr

60

65

70

AAT TTG GTG ATT TCT GAT ATA CTT TTT ACC ACG GCT TTG CCT ACA CGA 294

Asn Leu Val Ile Ser Asp Ile Leu Phe Thr Thr Ala Leu Pro Thr Arg

75

80

85

ATA GCC TAC TAT GCA ATG GGC TTT GAC TGG AGA ATC GGA GAT GCC TTG 342

Ile Ala Tyr Tyr Ala Met Gly Phe Asp Trp Arg Ile Gly Asp Ala Leu

90

95

100

TGT AGG ATA ACT GCG CTA GTG TTT TAC ATC AAC ACA TAT GCA GGT GTG 390

Cys Arg Ile Thr Ala Leu Val Phe Tyr Ile Asn Thr Tyr Ala Gly Val

105

110

115

FIG.1B-1

AAC TTT ATG ACC TGC CTG AGT ATT GAC CGC TTC ATT GCT GTG GTG CAC 438

Asn Phe Met Thr Cys Leu Ser Ile Asp Arg Phe Ile Ala Val Val His
 120 125 130 135

CCT CTA CGC TAC AAC AAG ATA AAA AGG ATT GAA CAT GCA AAA GGC GTG 486

Pro Leu Arg Tyr Asn Lys Ile Lys Arg Ile Glu His Ala Lys Gly Val
 140 145 150

TGC ATA TTT GTC TGG ATT CTA GTA TTT GCT CAG ACA CTC CCA CTC CTC 534

Cys Ile Phe Val Trp Ile Leu Val Phe Ala Gln Thr Leu Pro Leu Leu
 155 160 165

ATC AAC CCT ATG TCA AAG CAG GAG GCT GAA AGG ATT ACA TGC ATG GAG 582

Ile Asn Pro Met Ser Lys Gln Glu Ala Glu Arg Ile Thr Cys Met Glu
 170 175 180

TAT CCA AAC TTT GAA GAA ACT AAA TCT CTT CCC TGG ATT CTG CTT GGG 630

Tyr Pro Asn Phe Glu Glu Thr Lys Ser Leu Pro Trp Ile Leu Leu Gly
 185 190 195

GCA TGT TTC ATA GGA TAT GTA CTT CCA CTT ATA ATC ATT CTC ATC TGC 678

Ala Cys Phe Ile Gly Tyr Val Leu Pro Leu Ile Ile Ile Leu Ile Cys
 200 205 210 215

TAT TCT CAG ATC TGC TGC AAA CTC TTC AGA ACT GCC AAA CAA AAC CCA 726

Tyr Ser Gln Ile Cys Cys Lys Leu Phe Arg Thr Ala Lys Gln Asn Pro
 220 225 230

CTC ACT GAG AAA TCT GGT GTA AAC AAA AAG GCT CTC AAC ACA ATT ATT 774

Leu Thr Glu Lys Ser Gly Val Asn Lys Lys Ala Leu Asn Thr Ile Ile
 235 240 245

CTT ATT ATT GTT GTG TTT GTT CTC TGT TTC ACA CCT TAC CAT GTT GCA 822

Leu Ile Ile Val Val Phe Val Leu Cys Phe Thr Pro Tyr His Val Ala
 250 255 260

FIG.1B-2

ATT ATT CAA CAT ATG ATT AAG AAG CTT CGT TTC TCT AAT TTC CTG GAA 870
Ile Ile Gln His Met Ile Lys Lys Leu Arg Phe Ser Asn Phe Leu Glu
 265 270 275

TGT AGC CAA AGA CAT TCG TTC CAG ATT TCT CTG CAC TTT ACA GTA TGC 918
 Cys Ser Gln Arg His Ser Phe Gln Ile Ser Leu His Phe Thr Val Cys
 280 285 290 295

CTG ATG AAC TTC AAT TGC TGC ATG GAC CCT TTT ATC TAC TTC TTT GCA 966
Leu Met Asn Phe Asn Cys Cys Met Asp Pro Phe Ile Tyr Phe Phe Ala
 300 305 310

TGT AAA GCG TAT AAG AGA AAG GTT ATG AGG ATG CTG AAA CGG CAA GTC 1014
Cys Lys Gly Tyr Lys Arg Lys Val Met Arg Met Leu Lys Arg Gln Val
 315 320 325

AGT GTA TCG ATT TCT AGT GCT GTG AAG TCA GCC CCT GAA GAA AAT TCA 1062
 Ser Val Ser Ile Ser Ser Ala Val Lys Ser Ala Pro Glu Glu Asn Ser
 330 335 340

CGT GAA ATG ACA GAA ACG CAG ATG ATG ATA CAT TCC AAG TCT TCA AAT 1110
 Arg Glu Met Thr Glu Thr Gln Met Met Ile His Ser Lys Ser Ser Asn
 345 350 355

GGA AAG TGAATGCAT TGTATTTTGG TTTATAGTGA CGTAAACTGT ATGACAAACT 1166
 Gly Lys ***
 360

TTGCAGGACT TCCCTTATAA AGCAAAATAA TTGTTTCAGCT TCCAATTAGT ATTCTTTTAT 1226

ATTTCTTTCA TTGGGCGCTT TCCCATCTCC AACTCGGAAG TAAGCCCAAG AGAACAACAT 1286

AAAGCAAACA ACATAAAGCA CAATAAAAAT GCAAATAAAT ATTTTCATTT TTATTTGTAA 1346

FIG.1B-3

ACGAATACAC CAAAAGGAGG CGCTCTTAAT AACTCCCAAT GTAAAAAGTT TTGTTTTAAT 1406

AAAAAATTAA TTATTATTCT TGCCAACAAA TGGCTAGAAA GGAAGAATA GATTATATAT 1466

TGCCAGATGT TAATACTGTA ACATACTTTT TAAATAACAT ATTTCTTAAA TCCAAATTTT 1526

TCTCAATGTT AGATTTAATT CCCTCAATAA CACCAATGTT TTGTTTTGTT TCGTCTGGG 1586

TCATAAACT TTGTTAAGGA ACTCTTTTGG AATAAAGAGC AGGATGCTGC GGAATTC 1643

FIG.1B-4

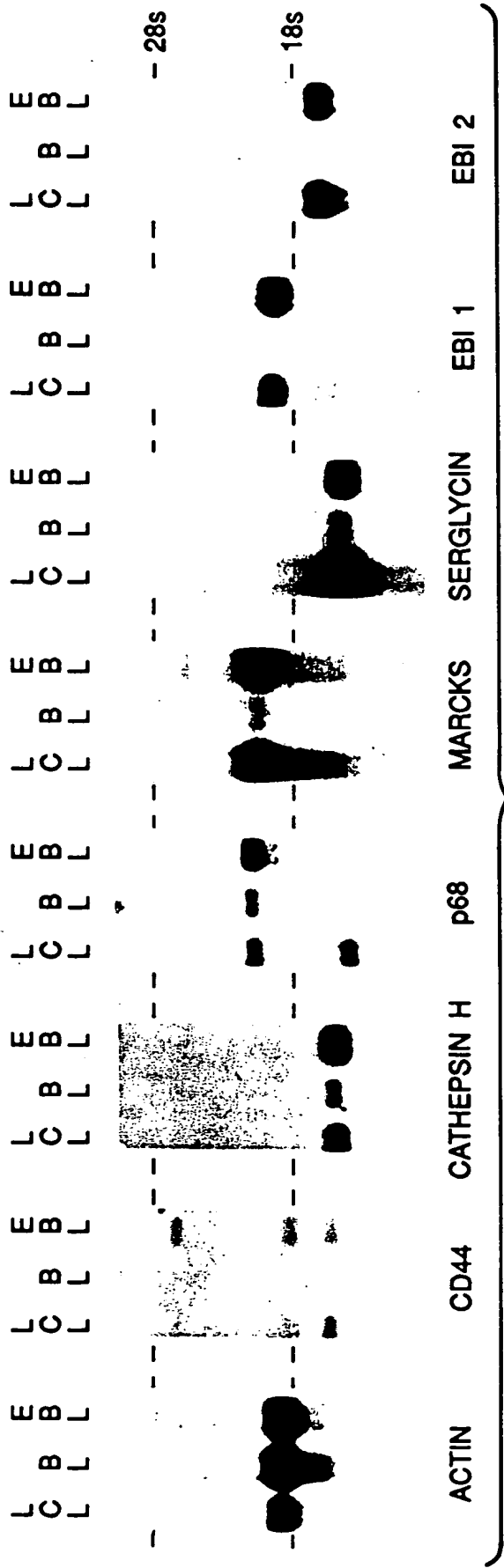
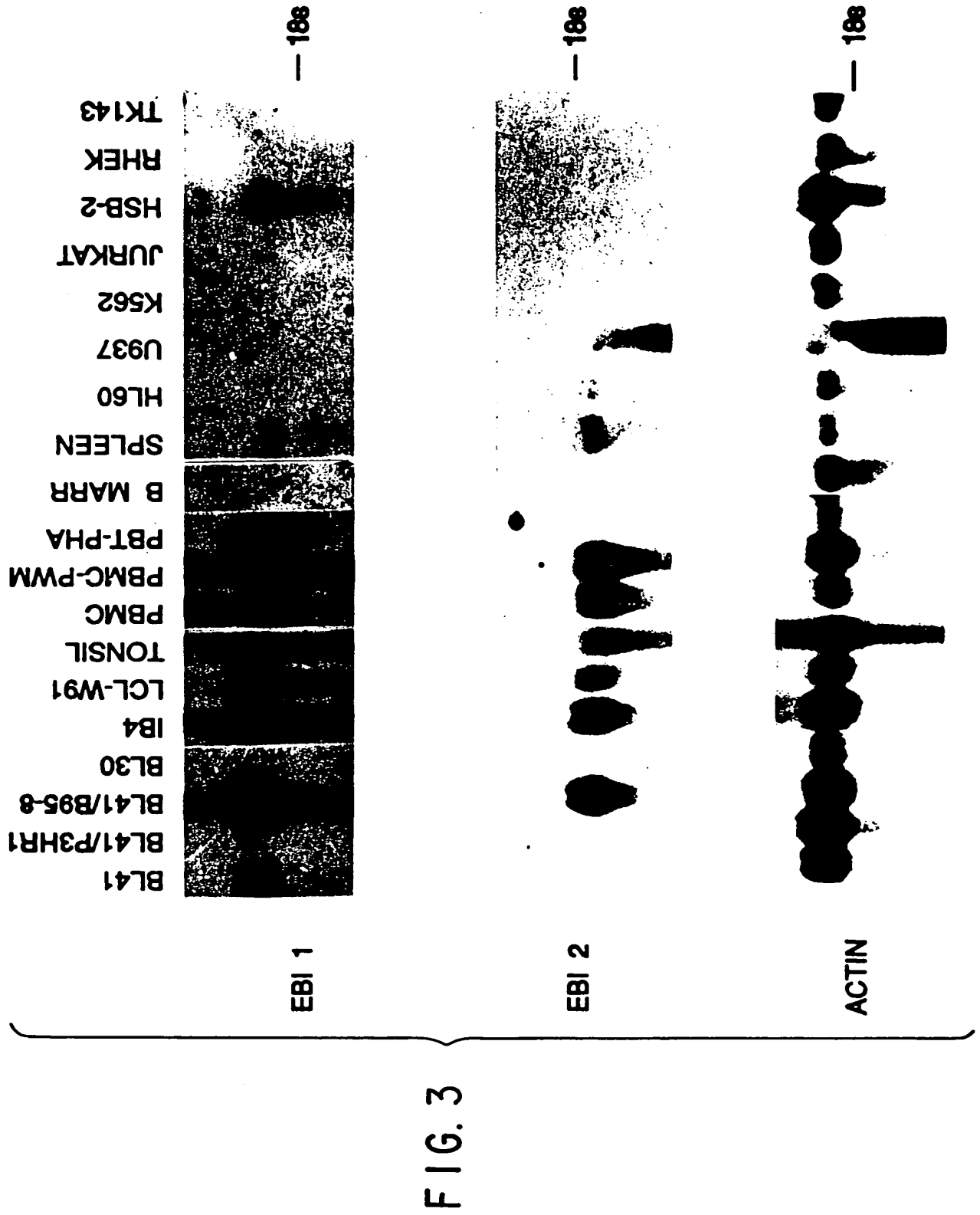


FIG. 2



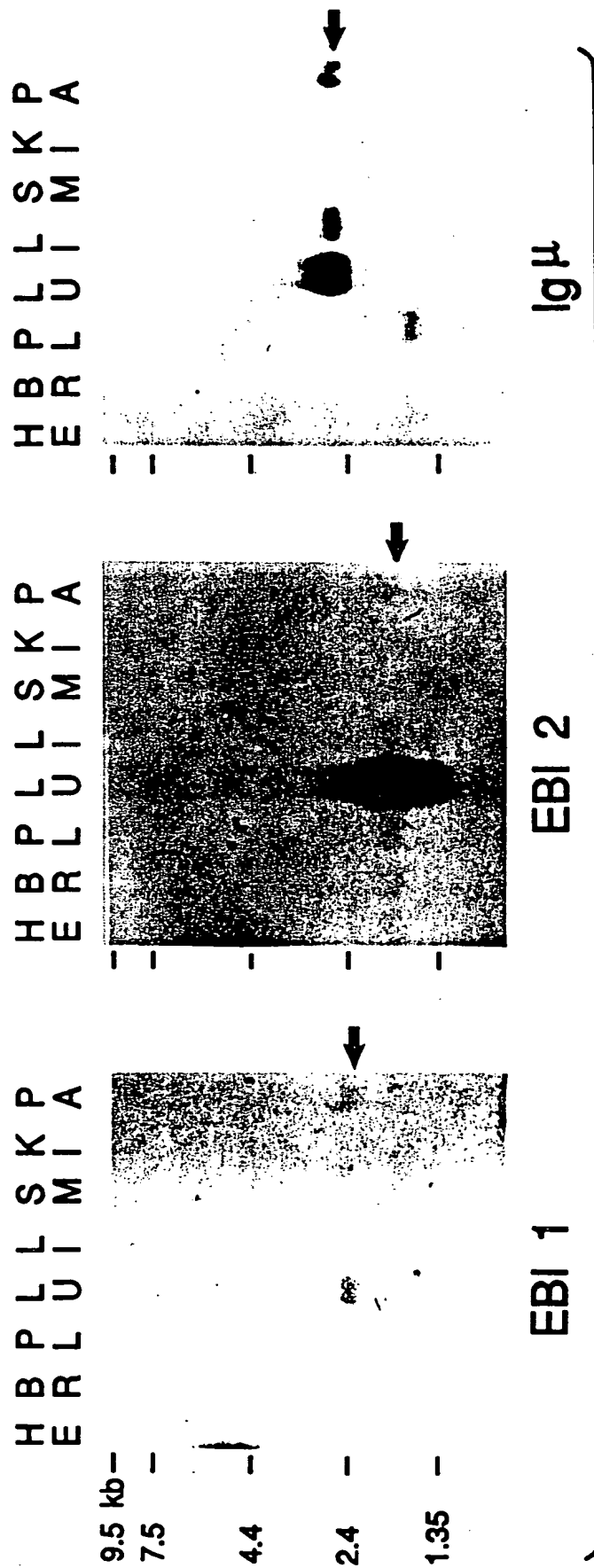


FIG. 4

GAATTCGCA GCC ATG ACC CCG CAG CTT CTC CTG GCC CTT GTC CTC TCG 49

Met Thr Pro Gln Leu Leu Leu Ala Leu Val Leu Trp
 1 5 10

GCC AGC TGC CCG CCC TGC AGT GGA AGG AAA GGG CCC CCA GCA GCT CTG 97

Ala Ser Cys Pro Pro Cys Ser Gly Arg Lys Gly Pro Pro Ala Ala Leu
 15 20 25

ACA CTG CCC CGG GTG CAA TGC CGA GCC TCT CGG TAC CCG ATC GCC GTG 145

Thr Leu Pro Arg Val Gln Cys Arg Ala Ser Arg Tyr Pro Ile Ala Val
 30 35 40

GAT TGC TCC TGG ACC CTG CCG CCT GCT CCA AAC TCC ACC AGC CCC GTG 193

Asp Cys Ser Trp Thr Leu Pro Pro Ala Pro Asn Ser Thr Ser Pro Val
 45 50 55 CHO ### ### 60

TCC TTC ATT GCC ACG TAC AGG CTC GGC ATG GCT GCC CGG GGC CAC AGC 241

Ser Phe Ile Ala Thr Tyr Arg Leu Gly Met Ala Ala Arg Gly His Ser
 65 70 75

TGG CCC TGC CTG CAG CAG ACG CCA ACG TCC ACC AGC TGC ACC ATC AGC 289

Trp Pro Cys Leu Gln Gln Thr Pro Thr Ser Thr Ser Cys Thr Ile Thr
 80 85 90

GAT GTC CAG CTG TTC TCC ATG GCT CCC TAC GTG CTC AAT GTC ACC GCC 337

Asp Val Gln Leu Phe Ser Met Ala Pro Tyr Val Leu Asn Val Thr Ala
 95 100 105 CHO ### ###

GTC CAC CCC TGG GGC TCC AGC AGC AGC TTC GTG CCT TTC ATA ACA GAG 385

Val His Pro Trp Gly Ser Ser Ser Ser Phe Val Pro Phe Ile Thr Glu
 110 115 120

CAC ATC ATC AAG CCC GAC CCT CCA GAA GGC GTG CGC CTA AGC CCC CTC 433

His Ile Ile Lys Pro Asp Pro Pro Glu Gly Val Arg Leu Ser Pro Leu
 125 130 135 140

FIG.5A

| | |
|---|-----|
| GCT GAG CGC CAC GTA CAG GTG CAG TGG GAG CCT CCC GGG TCC TGG CCC | 481 |
| Ala Glu Arg His Val Gln Val Gln Trp Glu Pro Pro Gly Ser Trp Pro | |
| 145 150 155 | |
| TTC CCA GAG ATC TTC TCA CTG AAG TAC TGG ATC CGT TAC AAG CGT GAG | 529 |
| Phe Pro Glu Ile Phe Ser Leu Lys Tyr Trp Ile Arg Tyr Lys Arg Gln | |
| 160 165 170 | |
| GGA GCT GCG CGC TTC CAC CGG GTG GGG CCC ATT GAA GCC ACG TCC TTC | 577 |
| Gly Ala Ala Arg Phe His Arg Val Gly Pro Ile Glu Ala Thr Ser Phe | |
| 175 180 185 | |
| ATC CTC AGG GCT GTG CGG CCC CGA GCC AGG TAC TAC GTC CAA GTG GCG | 625 |
| Ile Leu Arg Ala Val Arg Pro Arg Ala Arg Tyr Tyr Val Gln Val Ala | |
| 190 195 200 | |
| GCT CAG GAC CTC ACA GAC TAC GGG GAA CTG AGT GAC TGG AGT CTC CCC | 673 |
| Ala Gln Asp Leu Thr Asp Tyr Gly Glu Leu Ser Asp Trp Ser Leu Pro | |
| 205 210 215 220 | |
| GCC ACT GCC ACA ATG AGC CTG GGC AAG TAGCAAGGGC TTCCCGCTGC | 720 |
| Ala Thr Ala Thr Met Ser Leu Gly Lys *** | |
| 225 | |
| CTCCAGACAG CACCTGGGTC CTGCCACCC TAAGCCCCGG GACACCTGTT GGAGGGCGGA | 780 |
| TGGATCTGC CTAGCCTGGG CTGGAGTCCT TGCTTTGCTG CTGCTGAGCT GCCGGGCAAC | 840 |
| CTCAGATGAC CGACTTTTCC CTTTGAGCCT CAGTTTCTCT AGCTGAGAAA TGGAGATGTA | 900 |
| CTACTCTCTC CTTTACCTTT ACCTTTACCA CAGTGCAGGG CTGACTGAAC TGTCAGTGTG | 960 |

FIG.5B

AGATATTTTT TATTGTTTAA TTAGAAAAGA ATTGTTGTTG GGCTGGGCGC AGTGGATCGC 1020

ACCTGTAATC CCAGTCACTG GGAAGCCGAC GTGGGTGGGT AGCTTGAGGC CAGGAGCTCG 1080

AAACCAGTCC GGGCCACACA GCAAGACCCC ATCTCTAAAA AATTAATATA AATATAAAAT 1140

AAAAAAAAA AAAAGGAATT C 1161

FIG.5C

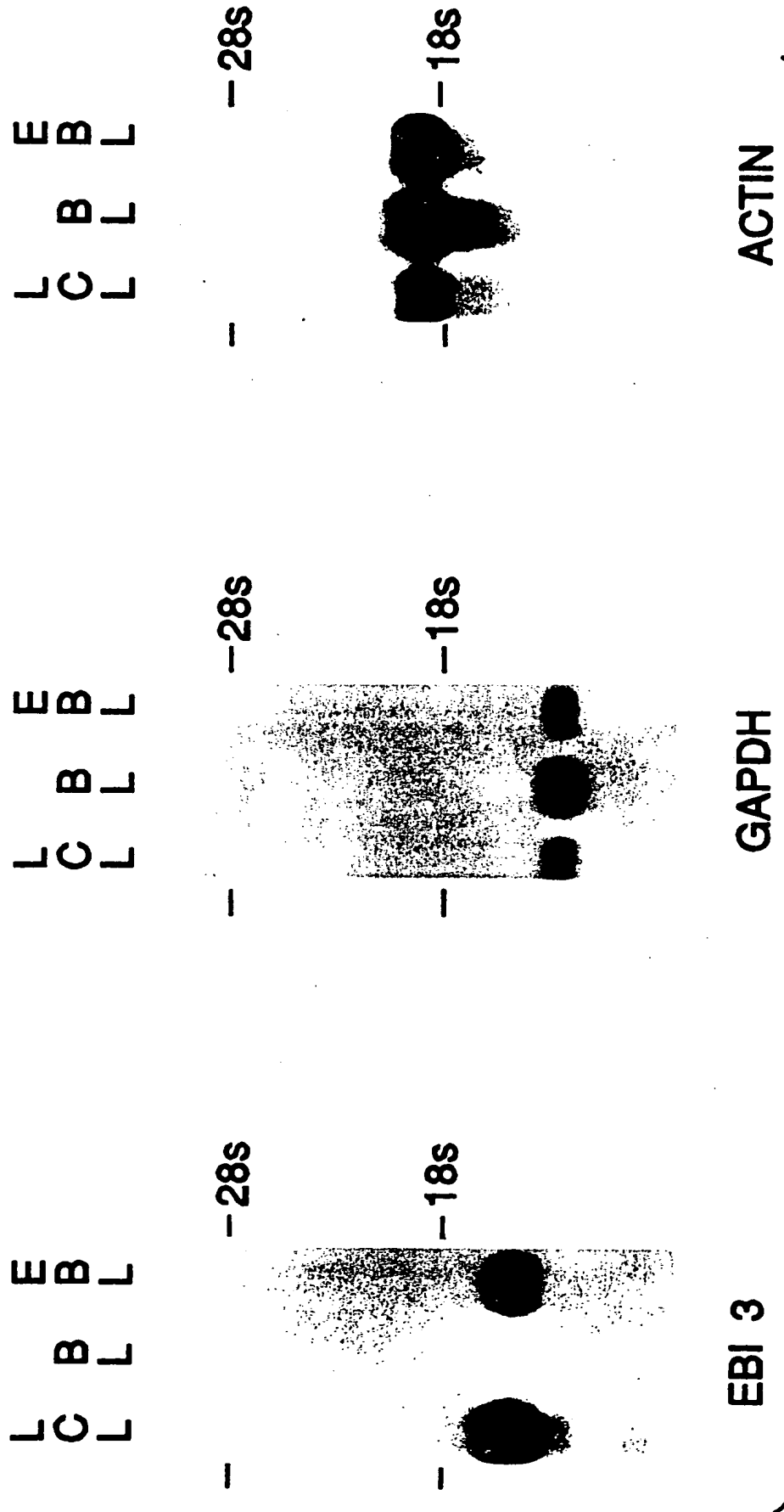
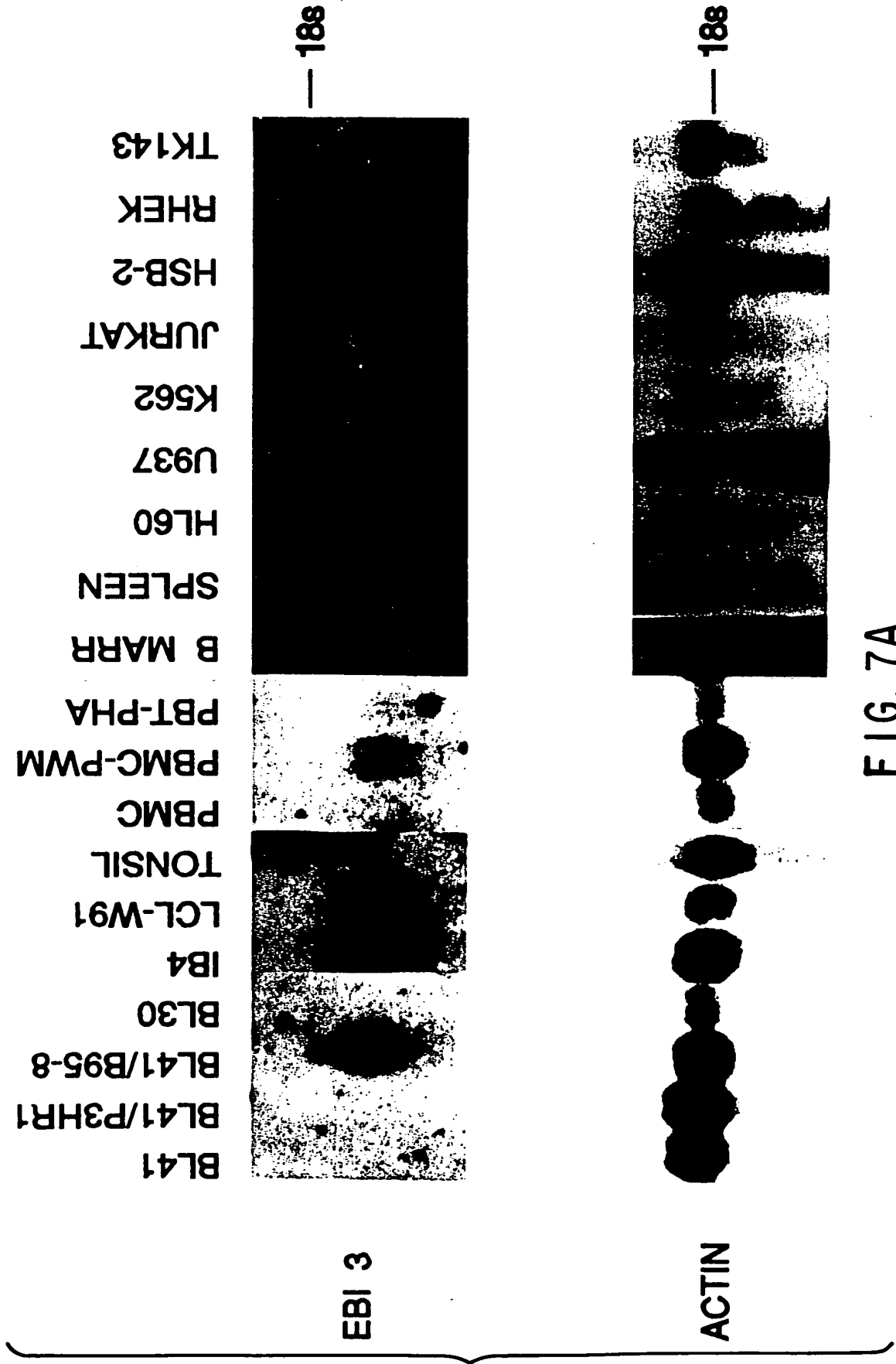


FIG. 6



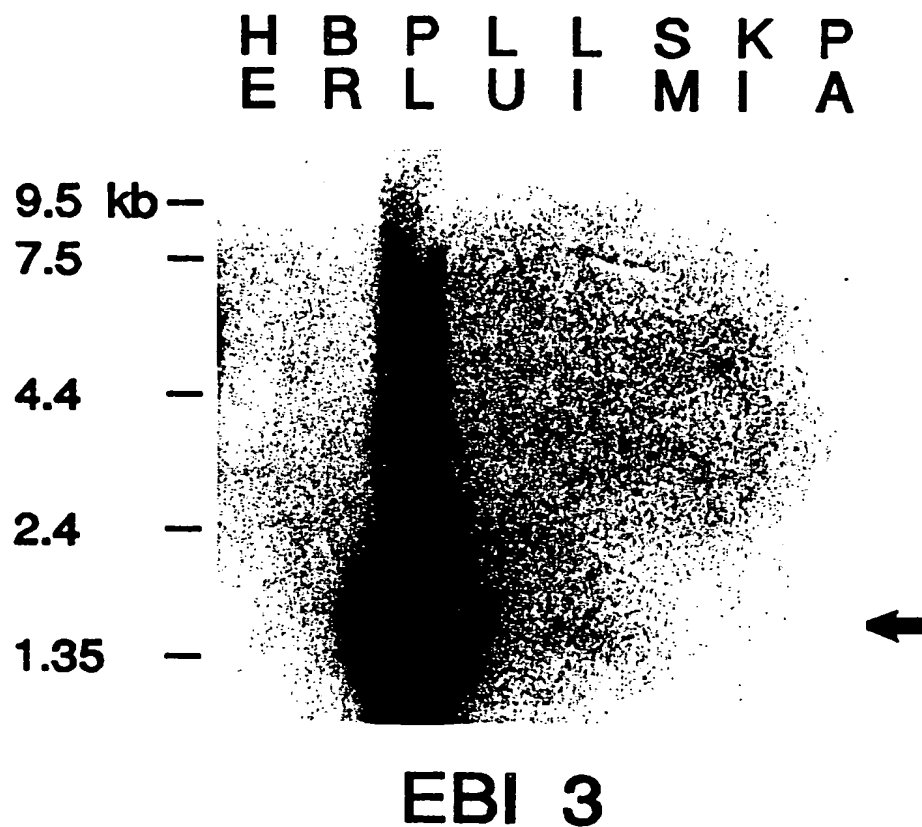


FIG. 7B